REMARKS

I. Status of the Claims

Claims 1-16, 18, 19, 23 and 25-27 are currently pending. Upon entry of this amendment, claims 3, 7, 14, 16, 23 and 25-27 are amended and claims 5 and 6 are cancelled without prejudice or disclaimer. Applicants reserve the right to reintroduce the unamended or cancelled claims in this or another application. New claims 28 and 29 are introduced upon entry of this amendment. Claims 1-4, 7-16, 18, 19, 23 and 25-29 are, thus, pending following entry of this amendment.

Claims 3, 7, 14, 23 and 25-27 are amended solely to address formal matters and, thus, do not narrow the scope of the claims.

New claim 28 is supported, for example, at page 4, lines 15-20, and page 17, lines 14-22. New claim 29 is supported, for example, by original claim 3.

II. Objections to the Claims

Claim 7 has been amended to delete one of the citations to SEQ ID NO:5, to insert the appropriate sequence identifiers, and to delete the reference to SEQ ID NO:106 as requested.

Claim 16 has been amended to depend only on claim 14.

III. Claim Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 3, 7 and 25-27 have been amended as requested to ensure proper antecedent basis. Claims 5 and 6 have been cancelled, thus rendering moot the rejection with respect to these claims.

Claims 14 and 16 have been amended to indicate that the hybridomas secrete rather than express an antibody as requested.

Claim 23 has been amended to consistently use the phrase "hybridoma cell" as requested.

IV. Amendments to the Specification

A paragraph describing the deposit of a number of hybridomas has been amended to correct a typographical error and to provide deposit dates and address information regarding the depository. These amendments introduce no new matter (see, e.g., MPEP 2406.01).

V. Claim Rejections under 35 U.S.C. § 112, First Paragraph

A. Deposits

Claim 15 is said not to be enabled because it is unclear whether the hybridomas recited in the claim have been deposited with an accepted public depository. Copies of deposit receipts from the European Collection of Cell Cultures (ECACC) are enclosed for each of the recited hybridomas. A declaration under 37 C.F.R. 1.808 is also enclosed stating that 1) each of the hybridomas has been deposited under the Budapest Treaty, 2) each hybridoma will be irrevocably and without restriction or condition released to the public upon issuance of a patent, and 3) that the deposits will be maintained in a public depository for a period of 30 years after the date of deposit, 5 years after the last request for a sample, or for the enforceable life of the patent, whichever is later.

B. Written Description

Claims 1-14, 16, 18-19 and 23 are rejected as encompassing subject matter that is said not to be adequately described in the specification. Applicants respectfully disagree for the following reasons.

Under the Written Description Guidelines (Fed. Reg., vol. 66, page 1106, January 5, 2001), the written description requirement can be satisfied in various ways, including: (1) actual reduction to practice, (2) reduction to drawings, or (3) disclosure of relevant identifying characteristics. This latter option can be achieved by: (a) disclosing structures or other chemical or physical properties, (b) functional characteristics coupled with a known or disclosed correlation between structure and function, or (c) combinations of such identifying characteristics.

Applicants submit that the specification adequately describes the current claims because it describes multiple antibodies that have actually been reduced to practice and also

provides a wealth of structural detail relevant to the claimed antibodies. The specification, for instance, describes 10 specific antibodies that fall within the scope of claim 1 (see, e.g., page 14, lines 26-34). This is a reasonable number of species to support the genus of antibodies claimed, for example, in claim 1, and satisfies criterion (1) above.

Furthermore, the specification provides complete sequences for a number of scFvs, as well as variable domains and CDRs, of antibodies having the activity recited in the claims. The application also provides an extensive description of what regions of certain sequences are tolerant to alteration and/or can be changed to improve certain desired properties of the antibodies (see, e.g., pages 38-56). Thus, the written description requirement is further satisfied on separate grounds by satisfying (3) above by disclosing structural details (i.e., sequences) of representative antibodies.

The written description rejection also conflicts with the Office's "Synopsis of Application of Written Description Guidelines" (Guidelines). Example 16 of the Guidelines analyzes whether a specification that characterizes an antigen X *but does not teach an example of antibodies which specifically bind to antigen X* nonetheless provides adequate written description for a broad claim reading: "[a]n isolated antibody capable of binding to antigen X."

The Guidelines conclude that the specification, even though it includes no examples of a specific antibody, nonetheless satisfies the written description requirement because the antigen is sufficiently characterized and because it is well known in the art how to make a variety of different types of antibodies to a defined antigen. Specially, the Guidelines state:

> Considering the routine art-recognized method of making antibodies to fully characterized antigens, the well define structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature, one of skill in the art would have recognized that the spectrum of antibodies which bind to antigen X were implicitly disclosed as a result of the isolation of antigen X.

Applicants submit that the specification adequately describes the current claims based upon the rationale set forth in Example 16 of the Guidelines because, like the exemplary claim in the example, the pending claims recite to antibodies that bind to a defined antigen, namely the factor IX forms recited in the claims. Moreover, the specification *exceeds* the description provided in Example 16 by describing the actual reduction to practice of multiple antibodies, whereas Example 16 assumes that the specification describes no actual reduction to practice but, nonetheless, concludes that the written description requirement is satisfied. It is, thus, submitted that the specification of the current application exceeds the written description requirements by analogy to the analysis provided in Example 16 of the Guidelines.

C. Enablement

Claims 1-14, 16, 18-19, 23 and 27 are rejected because the specification is said not to enable one of ordinary skill in the art to practice these claims without undue experimentation. For the reasons that follow, Applicants respectfully disagree.

With respect to the appropriate standard for evaluating whether undue experimentation is required to practice a claimed invention, the Federal Circuit in *In re Wands*, 8 USPQ2d 1400, 858 F.2d 731, 737 (Fed. Cir. 1988) stated:

> [E]xperimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art . . . *The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.* (emphasis added).

Based upon the foregoing standard set forth by the court, the currently claimed antibodies and antibody derivatives against factor IX/IXa can be prepared without undue experimentation and are, thus, enabled if *either* of two criteria are satisfied: 1) the antibodies can be prepared by "routine" experimentation, *or* 2) the specification provides a reasonable amount

of guidance with respect to the direction in which experimentation should proceed. Although only *one* of these criteria need be satisfied, Applicants submit that the specification satisfies *both*.

It is submitted, for instance, that the antibodies that are currently claimed can be prepared without undue experimentation because they can be prepared based upon the extensive discussion in the specification and methods that are routine in the art. Certain statements in Example 16 of the Guidelines referred to above illustrate the point that making antibodies to a specific antigen are routine in the art, stating, for example:

> The general knowledge in the art is such that antibodies are structurally well characterized . . . The sequences of constant regions as well as the variable regions subgroups (framework regions) from a variety of species are known and published in the art. It is also well known that antibodies can be made against virtually any protein . . . This is a mature technology where the level of skill is high and advanced.

For the foregoing reasons, Applicants, thus, submit that antibodies to the forms of Factor IX recited to in the claims could be prepared without undue experimentation.

It would also have been routine as of the priority date of the application to identify specific antibodies from this group that exhibited the desired ability, namely the ability to increase the procoagulant activity of factor IX (e.g., antibodies with Factor VIII-like activity). Such screening methods would be routine because a number of assays for Factor VIII activity were known, including commercially available assays and even high throughput screening methods (see, e.g., the one step coagulation test or chromogenic tests; see, e.g., page 18, lines 20-30.) The specification also describes assays for Factor VIII-like activity in detail in examples 2 and 4.

Because one of ordinary skill could have *routinely* prepared antibodies or antibody derivatives to the factor IX forms recited to in the claims and *routinely* screened such antibodies using conventional assays in the art as of the priority date of the application, criterion 1 listed above is satisfied. This by itself is sufficient to establish that the current claims are enabled.

Nonetheless, criterion 2 listed above is also satisfied, because the specification provides considerable guidance regarding the preparation of the claimed antibodies. The specification, for instance, provides extensive discussion regarding methods of preparing the claimed antibodies (see, e.g., pages 15-20). Examples detailing the production of antibodies is also provided (examples 2 and 3). Furthermore, to reiterate a point made above, the specification also provides the complete sequence scFvs, variable domains and CDRs, and provides guidance on what regions can be mutated. This extensive guidance more than satisfies the requirement of criterion 2, namely that the specification provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. This is particularly true given the statements in Example 16 of the Guidelines noting that antibodies are structurally well characterized and that sequences of constant and variable regions from a variety of species are known in the art. For all these reasons, criterion 2 is also satisfied.

Applicants also point out that the antibodies that are claimed unexpectedly have FVIII-like activity, which constitutes a totally new achievement. It was unexpected to be able to obtain antibodies such as currently claimed because the expectation would be that antibodies to Factor IX would *inhibit* the protein, whereas the claimed antibodies *activate* the recited forms of Factor IX. This surprising result opens up new and important potential applications for these antibodies. Because of this significant contribution to the art, the scope of the claim is deemed justified.

VI. Claim Rejections under 35 U.S.C. § 102

Claims 1-6, 14, 16, 18, 23, 25 and 27 are said to be anticipated by U.S. Patent 6,391,299 to Blackburn et al. ("Blackburn"). Applicants respectfully disagree with this conclusion because Blackburn fails to disclose each and every element of the claimed invention as required for an anticipation rejection.

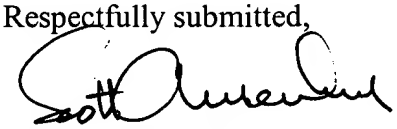
The Office acknowledges that Blackburn does not teach or suggest antibodies that increase the activity of Factor IXa as required by the rejected claims. The Office tries to avoid this deficiency by arguing that such activity is an inherent property of the antibodies discussed in Blackburn. Applicants disagree because, as acknowledged in the Office Action itself, the

antibodies discussed in Blackburn inhibit thrombosis (i.e., inhibit coagulation; see e.g., abstract). The claimed antibodies, in contrast, increase procoagulation activity. The antibodies discussed in Blackburn, thus, have the *opposite* activity of the claimed antibodies and support Applicants' position articulated above, namely that it was unexpected to be able to obtain antibodies against Factor IX/IXa that increase rather than inhibit the procoagulant activity of FIXa.

VII. Conclusion

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,



Date: July 2, 2004

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